Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Peripheral and Central Nervous System Drugs Advisory Committee Meeting
October 14, 2009

Topic: The committee discussed new drug application (NDA) 22-250, with the proposed trade name AMPRIVA (fampridine) 10 milligram (mg) tablets, manufactured by Acorda Therapeutics, Inc. The proposed indication for this new drug product is to improve walking ability in individuals with multiple sclerosis (MS). MS is a neurological disease that may cause a wide variety of possible symptoms, including in some patients difficulty in walking.

These summary minutes for the October 14, 2009 Peripheral and Central Nervous System Drugs Advisory Committee meeting were approved on October 22, 2009.

I certify that I attended the October 14, 2009 Peripheral and Central Nervous System Drugs Advisory Committee meeting and that these minutes accurately reflect what transpired.

_____*-signed-*_____
Diem-Kieu H. Ngo, Pharm.D., BCPS
(Designated Federal Official)

_____*-signed-*_____
Britt Anderson, M.D., Ph.D.
(Acting Chair)

Summary Minutes of the Peripheral and Central Nervous System Drugs Advisory Committee Meeting
October 14, 2009

The following is the final report of the Peripheral and Central Nervous System Drugs Advisory Committee meeting held on October 14, 2009. A verbatim transcript will be available in approximately six weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PeripheralandCentralNervousSystemDrugsAdvisoryCommittee/ucm126190.htm.

All external requests for the meeting transcripts should be submitted to the CDER Freedom of Information Office.

The Peripheral and Central Nervous System Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on October 14, 2009 at The Inn and Conference Center, University of Maryland University College (UMUC), Marriott Conference Centers 3501 University Blvd. East, Adelphi, Maryland. Prior to the meeting, the members and temporary voting members were provided the background materials from the FDA and Acorda Therapeutics, Inc. The meeting was called to order by Britt Anderson, M.D., Ph.D. (Acting Chair); the conflict of interest statement was read into the record by Diem-Kieu H. Ngo, Pharm.D., BCPS (Designated Federal Official). There were approximately 150 people in attendance. There were eleven Open Public Hearing (OPH) speakers.

Issue: The committee discussed new drug application (NDA) 22-250, with the proposed trade name AMPRIVA (fampridine) 10 milligram (mg) tablets, manufactured by Acorda Therapeutics, Inc. The proposed indication for this new drug product is to improve walking ability in individuals with multiple sclerosis (MS). MS is a neurological disease that may cause a wide variety of possible symptoms, including in some patients difficulty in walking.

Attendance:
Peripheral and Central Nervous System Drugs Advisory Committee members present (voting): Britt Anderson, M.D., Ph.D. (Acting Chair); Mark W. Green, M.D.; Stacy A. Rudnicki, M.D.

Peripheral and Central Nervous System Drugs Advisory Committee members absent (voting): Ying Lu, Ph.D.; Gregory L. Holmes, M.D; Sandra F. Olson, M.D.

Drug Safety and Risk Management Advisory Committee members present (voting): Elaine H. Morrato, Dr.P.H.; Sidney M. Wolfe, M.D. (Acting Consumer Representative)

Temporary Voting Members: Cynthia Sitcov (Patient Representative); Gerald van Belle, Ph.D.; Jason W. Todd, M.D.; Steven D. Brass, M.D., M.P.H.; Myla D. Goldman, M.D., M.Sc.; Olaf Stuve, M.D. (*via telephone*), Ph.D.; Nathan B. Fountain, M.D.; Eluen A. Yeh, M.D.

Industry Representative present (non-voting): Roy E. Twyman, M.D.

FDA Participants (non-voting): Robert Temple, M.D.; Russell G. Katz, M.D.; Eric Bastings, M.D.

Open Public Hearing Speakers: Nicholas G. LaRocca, Ph.D.; June Halper; Susan Zurndorfer; Karen Knable Jackson; Elissa (EJ) Levy; Robert B. Engel; Jacqueline Havener; Christopher T. Bever, Jr., M.D., M.B.A.; Serena Lowe; Diane Edquist Dorman; Jonathan and Mimi Mosher

The agenda was as follows:

8:00 a.m.	*Call to Order and Opening Remarks*	***Britt Anderson, M.D., Ph.D.*** *Acting Chair* *Peripheral and Central Nervous System Drugs Advisory Committee*
	Introduction of Committee	
	Conflict of Interest Statement	***Diem-Kieu H. Ngo, Pharm.D., BCPS*** *Designated Federal Official*
8:15 a.m.	*FDA Introductory Remarks*	***Russell Katz, M.D.*** *Director, Division of Neurology Products (DNP)* *Office of Drug Evaluation I, OND, CDER, FDA*
8:30 a.m.	***INDUSTRY PRESENTATION*** *Fampridine-SR for Improved Walking Ability in Patients with Multiple Sclerosis*	
	Background and Introduction	***Ron Cohen, M.D.*** *President and CEO, Acorda Therapeutics*
	Medical Need and Outcome Measures	***Aaron Miller, M.D.*** *Corinne Goldsmith Dickinson Center for Multiple Sclerosis and Professor of Neurology Mount Sinai School of Medicine, New York, NY*
	Clinical Program: Efficacy	***Andrew Blight, Ph.D.*** *Chief Scientific Officer, Acorda Therapeutics*
	Clinical Program: Safety	***Thomas Wessel, M.D., Ph.D.*** *Chief Medical Officer, Acorda Therapeutics*
	A Clinical Perspective *Rehabilitation*	***Christine Short, M.D.*** *Division Chief, Physical Medicine and Assistant Professor, Department of Medicine* *Dalhousie University, Halifax, Canada*
	Benefit-Risk	***Aaron Miller, M.D.*** *Corinne Goldsmith Dickinson Center for Multiple Sclerosis and Professor of Neurology Mount Sinai School of Medicine, New York, NY*
10:00 a.m.	*Clarifying Questions*	
10:15 a.m.	***BREAK***	

FDA PRESENTATION

10:30 a.m.	*Fampridine Efficacy Issues*	***Kachikwu Illoh, M.D., M.P.H.*** *Medical Officer, Division of Neurology Products* *Office of Drug Evaluation I, OND, CDER, FDA*
10:50 a.m.	*Fampridine and Seizure Risk*	***Gerard Boehm, M.D., M.P.H.*** *Medical Officer, Division of Neurology Products* *Office of Drug Evaluation I, OND, CDER, FDA*
11:15 a.m.	*Clarifying Questions*	
11:30 a.m.	***LUNCH***	
12:30 p.m.	*Open Public Hearing*	
1:30 p.m.	*Panel Discussion/Questions*	
3:00 p.m.	***BREAK***	
3:15 p.m.	*Panel Discussion/Questions*	
5:00 p.m.	*Adjournment*	

Questions to the Committee:

1. Has the sponsor demonstrated substantial evidence of effectiveness of fampridine as a treatment to improve walking in patients with multiple sclerosis (MS)? YES/NO/ABSTAIN

   YES: 12 NO: 1 ABSTAIN: 0

   Committee Discussion: *Dr. Katz clarified that "substantial" is a regulatory term that is defined as "evidence from adequate and well controlled trials" as some of the panel members were unclear of what constitutes "substantial evidence".*

   a. If yes, has the sponsor demonstrated that this effect is clinically meaningful, either in the group of fampridine-treated patients as a whole, or in a specific subset? DISCUSSION

   Committee Discussion: *Panel members who did not feel there was a clinically meaningful effect placed emphasis on treated vs. untreated groups as a whole and the lack of a difference between walking speed in the treated group vs. untreated group as a basis for this decision. Some panel members also use the proportion of responders and prior demonstration of responders' subjective impression as a basis for their decision. Other panel members also emphasized the proportion of changes in walking speed and walking time to reach their conclusion of clinically meaningfulness of the effect.*

2. If yes to question #1, should the sponsor be required to evaluate the effects of doses lower than 10 mg twice daily (BID)? YES/NO/ABSTAIN

   YES: 12 NO: 1 ABSTAIN: 0

a. If yes, should this be required prior to approval? YES/NO/ABSTAIN

YES: 2 NO: 11* ABSTAIN: 0

Committee Discussion: *The majority of the committee agreed that doses lower than 10 mg twice daily should be evaluated to see if seizure risk and other adverse events are decreased while still maintaining efficacy, thus improving the benefit to risk ratio. The majority of the committee also agreed that the requirement of studies of lower dosages should not prohibit the approval of the product at the proposed 10 mg twice daily dosing.*

***NOTE: One panel member did not place a vote in the electronic voting system; however, the panel member verbally stated her vote as "NO".**

3. If substantial evidence of a clinically meaningful effect has been demonstrated, do you conclude that there are conditions under which fampridine SR could be considered safe in use for this indication? YES/NO/ABSTAIN

YES: 10 NO: 2 ABSTAIN: 1

a. If yes, what are those conditions (e.g., specific enrollment criteria, specific monitoring, etc.)? DISCUSSION

Committee Discussion: *The committee was in agreement that fampridine should not be used in patients with moderate to severe renal insufficiency (baseline serum creatine or creatinine clearance should be obtained) and in patients with known seizure disorder or are at high risk for seizures. The committee also expressed a view that there is no need for pre-screening EEG before initiation of fampridine as there is no clinical evidence to support the use of EEG to predict seizure risk.*

The meeting was adjourned at approximately 5:00 p.m.